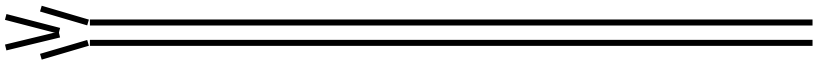
Chapter 5



Method Approval Process

5.1 Introduction

Two principal objectives of the streamlining initiative are to encourage organizations external to EPA to develop and submit for approval new analytical methods and to expedite method approval at 40 CFR parts 136 and 141. The key to the success of these efforts is to define procedures and provide guidance to the public on how to develop, validate, and submit a method to EPA for approval. This guidance is intended to encourage participation of external organizations in method development. Additionally, it will expedite the method approval process by ensuring that methods submitted to EPA for approval are in the correct format, have been appropriately validated, and are accompanied by the necessary supporting documentation.

This chapter details the procedures for preparing and submitting method documentation under the streamlining initiative, and describes the rulemaking process required to approve a new method or method modification. By providing increased method flexibility as described in Chapter 2 of this guide, EPA expects to significantly reduce the number of modified methods that must undergo rulemaking as alternate test procedures (ATPs), while increasing the number of new methods submitted for approval. Under the streamlining initiative, all new methods will be subject to EPA review and approval. Modified methods at validation Tiers 2 and 3 will be reviewed and approved by EPA only if requested. EPA approval may take the form of a letter of approval or a rulemaking to propose the method at 40 CFR part 136 or part 141, as described in this chapter.

The key concepts presented and discussed in this chapter are*: method development, standard EPA method format, rulemaking process, direct final rulemaking, proprietary reagents, proprietary instruments, and proprietary methods.*

5.2 Pre-Submission Procedures

Under streamlining, EPA must review all new methods, and will review Tier 2 and Tier 3 method modifications upon request. Prior to submitting a method to EPA for review, a party developing a new or modified method will undertake several preparatory activities: method development, method validation, and, if a rulemaking will occur, compilation of preamble information. Method developers also may wish to publish their method independently.

5.2.1 Method Development

Any party who identifies a new or improved procedure or technique for analyzing an analyte of interest can develop a new method or method modification. A new method must be a unique combination of analyte and determinative technique, as discussed in Chapter 2. Otherwise, it would

qualify as a modification of an existing method. In addition, the determinative technique in a new method must be more sensitive and/or selective (specific) than the determinative techniques in all methods previously approved for the analyte. Further, a new method must include the standardized QC elements and specify QC acceptance criteria for each required QC element. The QC acceptance criteria must be developed from data gathered in the method validation study, as described in Chapter 3 of this guide.

The **method development** process will typically include drafting the method, and checking, modifying, and rechecking testing procedures. If an interlaboratory study is required to validate the method, generally a single-laboratory study is done during the method development phase to identify method revisions needed preceding the interlaboratory study. The method should be written in the **standard EPA method format**. EPA method format requirements are specified in *Guidelines and Format for Methods to be Proposed at 40 CFR Part 136 or Part 141* (Guidelines and Format). The Guidelines and Format document incorporates the analytical methods format prescribed by EPA's Environmental Monitoring Management Council (EMMC). An objective of the EMMC format is to standardize all Agency analytical methods.

A standardized method format used by a government agency such as the U.S. Geological Survey or a consensus standards organization such as Standard Methods, ASTM, or AOAC-International can be used by those organizations, in lieu of the EPA format. However, these formats may be used only by these organizations to avoid possible confusion over authorship. Other parties are required to use the standard EPA format. EPA will review and approve standardized formats from governmental authorities and industrial associations upon request, but will not approve miscellaneous formats written by instrument manufacturers, individual laboratories, and others, because of the potential proliferation of different method formats. EPA believes that the format provided in Guidelines and Format is more than adequate to meet the needs of the analtyical community.

5.2.2 Method Validation

Each new method or method modification must be tested to assess its performance. The process of establishing or substantiating method performance is called validation. Method validation requirements are described in Chapter 4. The method developing organization is responsible for performing the validation study at the appropriate validation tier, according to the procedures described in Chapters 4. A validation study plan should be prepared prior to the study; the results of the study must be detailed in a method validation report. The contents of the method validation report and the supporting Checklists and data that must accompany the report are specified in Chapter 4.

5.2.3 Compilation of Information to Support Development of Preamble

When methods will undergo the rulemaking process, the method submitter must compile information on the method that will facilitate EPA preparation of a draft preamble for proposal of the method at 40 CFR parts 136 or 141. Information that should be provided includes: a detailed summary of the method, a discussion of QC acceptance criteria development, and a description and discussion of the interlaboratory method validation study and any other method studies conducted during method development and validation.

When preparing method information, the method submitter must:

- Define the purpose and intended use of the method.

- State what the method is based upon, noting any relationship of the method to other existing analytical methods. Indicate whether the method is associated with a sampling method.

- List analytes that can be measured by the method, including each analyte's Chemical Abstracts Service Registry Number (CASRN). If regulations cite other than the most commonly used analyte name, refer to the regulation. For pesticides, use "acceptable common names." The use of registered trade names is permitted.

- Identify the matrix(ces) for which the method has been found satisfactory.

- Indicate the statistically determined method detection limit (MDL) and the analyte concentration range over which the method is applicable. State the matrix(ces) in which MDL was determined. If the MDL is not available, report an instrumental detection limit and define how it was derived. Indicate the minimum level (ML) and water quality criteria if appropriate to the analyte and method.

- Describe method limitations, such as "This method is not applicable to saline water," or "This method is not intended for determination of metals at concentrations normally found in treated and untreated discharges from industrial facilities." Indicate any means of recognizing cases where the method may not be applicable to the sample under test.

- Outline, specifying amounts of sample and reagent, the procedure that is followed to determine the presence or absence of the listed analytes. Include any sample pretreatment, such as filtration or digestion. In this description, identify the basic steps involved in performing the method, but omit the details that are a necessary part of the complete statement of procedure.

- State the type of procedure (colorimetric, electrometric, volumetric, etc.) and describe the source of color, major chemical reaction, including pertinent chemical equations, etc. For instrumental methods, state the technique.

- Identify the determinative step in the method.

- List options to the method, if applicable.

- Discuss in a summary fashion how quality is assured in the method. For new methods, describe and discuss the development of QC acceptance criteria for all of the standard QC elements. For modified methods, include a discussion that compares the method results to the QC acceptance criteria of the reference method.

- Describe and discuss the method validation study and the study results, including study design and objectives, study limitations, study management, technical approach, data reporting and validation, results, data analysis discussion, and conclusions.

- Describe and discuss any MDL studies or other method studies that were conducted during method development and validation

Looking at previous method rules provides an idea of the type of method information and the appropriate level of detail for submitting method information to EPA. Examples of preambles for

method rules include: 49 *FR* 43234, October 26, 1984; 56 *FR* 5090, February 7, 1991; 60 *FR* 53988, October 18, 1995; and 61 *FR* 1730, January 23, 1996.

5.2.4 Method Publication

An objective of the streamlining initiative is to incorporate methods by reference in proposals. EPA is working with the Office of the Federal Register (OFR) to accomplish this objective. Incorporation by reference would facilitate method updates, increase the accessibility of the method, and save on publication costs. To support incorporation by reference, it would be helpful if the method developing organization published the method. Method approval requests submitted by governmental authorities or industrial associations should meet this requirement without difficulty. Vendors, laboratories and other small parties may be unable to undertake direct publication. A possible solution for small parties wishing to incorporate their methods by reference is to have the methods published by the National Technical Information Service (NTIS) or the Educational Resources Information Center (ERIC). If suitable means of publication are not available, particularly to small business submitters, EPA may assist in having the method published by NTIS or ERIC.

5.3 Submission of Method Approval Applications to EPA

When the pre-submission steps are completed, the method submitter must compile and submit to EPA a method approval application package. The method approval application package will be submitted to the Analytical Methods Staff (AMS), within EPA's Office of Water. The application package will contain the method validation study report, including the formatted method and supporting data. Requirements for the method validation study report and supporting documentation are specified in section 4.6. If the method will undergo rulemaking, the application package also must include information to facilitate EPA preparation of a draft preamble as described in section 5.2.3.

5.4 EPA Review of Method Approval Applications

EPA will review all new methods, and will review Tier 2 and Tier 3 method modifications if requested. When a method package is submitted for review, EPA will first check the documentation for completeness. If all of the documentation is in order, EPA will begin an internal review of the method for scientific merit, consistency, and appropriateness. If documentation is incomplete, EPA will contact the submitter and request submission of missing documentation before proceeding with its review.

The internal review at EPA may involve multiple programs and workgroups. Should any problems or questions arise, EPA will communicate with the submitter to resolve the outstanding issues. Depending on the circumstances, EPA may return the application to the submitter for revision.

If internal reviewers recommend approval of the new method or method modification, EPA will issue a letter of acceptance for a Tier 1 new method. For Tier 2 and Tier 3 new methods, EPA will begin the rulemaking process. For Tier 2 and Tier 3 method modifications, the method submitter has the option of receiving a letter of approval or proceeding with the rulemaking process.

Table 5-1: EPA Review and Action for New and Modified Methods

	New Method	Modified Method
Tier 1 Single-lab, single matrix type/single PWS	• EPA review required • EPA issues a letter of approval	• No EPA review
Tier 2 Multi-lab, single matrix type/all PWSs	• EPA review required • Approved through rulemaking	• If requested, EPA reviews and - issues letter of approval, or - conducts rulemaking
Tier 3 Multi-lab, all matrix types	• EPA review required • Approved through rulemaking	• If requested, EPA reviews and - issues letter of approval, or - conducts rulemaking

5.5 Tier 1/Single-Laboratory Use Methods

Under the streamlining initiative, EPA proposes to allow use of single-laboratory, limited-use methods as Tier 1 methods for both wastewater and drinking water. This will provide the means by which (1) a new technology can be introduced, and (2) specific matrix interference problems can be overcome. Further, additional single laboratories can use the technology until a sufficient number of devices are available for interlaboratory validation.

Currently, EPA reviews single-laboratory, limited-use methods only for special applications. Examples of special circumstances could include procedures to remove sulfate interferences in drinking water matrices and, as described below, technologies that can eliminate total cyanide false positives in some wastewater measurements. Under streamlining, EPA will review and issue letters of approval for Tier 1 new methods. Tier 1 modified methods can be used once they are validated and documented in accordance with EPA guidelines (see method validation guidelines in Chapter 4). EPA will not review Tier 1 method modifications.

EPA recognizes that allowing single-laboratory use of a new technology for regulatory compliance carries with it the risk that results produced with the new technology may not agree with results produced by an approved method. However, EPA believes that there can be a net benefit to the regulated community by allowing new technologies that can overcome matrix interference problems. For example, it is known that methods that measure total cyanide are susceptible to interferences from thiosulfates and other substances, and certain members of the regulated industry have pointed out to EPA that they have been faced with permit violations caused by these interferences. A new technology involving flow-injection and ligand-exchange has been demonstrated to overcome many of the matrix interferences in the determination of cyanide. Upon application by a discharger, and provided that the method could be demonstrated by the discharger to overcome the matrix interference problem, EPA would grant approval for use of the method on the particular discharge. After a sufficient number of dischargers utilized the new technology, the method employing the technology could be validated in an interlaboratory study then proposed for listing in Table IB at 40 CFR part 136.3.

Although method modifications do not require formal approval, Tier 1 new methods must be submitted to EPA for review. Upon recommendation for approval, a letter of approval will be issued. Tier 1 modified methods can be used directly upon verification. EPA will not review Tier 1 method modifications.

5.6 Rulemaking Process

The customary **rulemaking process** consists of four phases: 1) proposal of the rule, 2) public comment, 3) response to comments, and 4) publication of the final rule. The proposed rule requests public comment and allows a specified comment period, for example 30 to 90 days depending on the magnitude of the proposed change. At the end of the comment period, EPA will forward any significant comments to the method submitter. The submitter would then provide technical assistance to EPA in drafting responses to comments. All comments that have scientific or legal merit, or raise substantive issues with the proposed rule, must be answered to complete the rulemaking process.

EPA will review the comment responses and complete a response-to-comments document that must be included in the final rule. EPA will prepare and submit the final rule to the OFR for publication. The final rule will state the date that the rule becomes effective, typically 30 days after rule publication. As of this date, the method is approved.

EPA plans to use a **direct final rulemaking** process to expedite the approval of noncontroversial updates to methods, such as revisions to currently approved methods published by EPA, other government agencies, and consensus standards organizations. Direct final rules are warranted when it is not in the public interest to delay approval of the action and when the action is not expected to elicit public comment to which the Agency would be required to respond.

The direct final rulemaking process was designed to accelerate the approval of noncontroversial rules. In this process, the rule is published only once, because the proposed and final rules are considered to be published simultaneously as a “direct final rule” in the Federal Register. The proposed rule has a specific comment period (typically 60 days after FR publication) and the final rule has a later effective date (typically 120 days after FR publication). If no comments that would normally require an official Agency response are received during the comment period, the final rule becomes effective.

If comments requiring a response are received during the comment period, the Agency must take one of two actions before the effective date. The Agency can publish a Federal Register notice withdrawing all or part of the action, or the Agency can publish another final rule within the 120-day period. This final rule would include the Agency's response to comments and final action on the proposed action with a new effective date for updating the CFR. If a second final rule must be prepared, the submitting party (e.g., consensus standards organization) would be required to provide EPA with technical assistance in preparing the response to comments before the final rule could be published.

Direct final rulemaking saves time and Agency resources. For example, based on the example time periods given in this section, if no adverse comments are received, a direct final rule would become effective within 120 days of publication (i.e., the CFR tables would be updated on the 120-day effective date).

5.7 Proprietary Reagents, Instruments, and Methods

EPA separates proprietary components into three categories: proprietary reagents, proprietary instruments, and proprietary methods. EPA intends to attempt to accommodate the inclusion of **proprietary reagents** and **proprietary instruments** in the approval of analytical methods for compliance purposes to the extent that such inclusion still provides an adequate opportunity for public review and comment under the Administrative Procedure Act. EPA does not anticipate, however, that it could approve the use of **proprietary methods** for determining compliance with regulatory requirements where the entire method is claimed as "confidential business information" because the opportunity for public review and comment might be restricted too severely. If a proprietary method is patented, the method would be considered for approval as a compliance method because the public would be able to comment on the patented method. EPA believes the restriction on approval of proprietary methods is not serious because reagents or instruments, not complete methods, will continue to be the most common proprietary components used in compliance methods.

Proprietary reagents and instruments are currently included for use in approved methods and would continue to be allowed in approved methods. The details of the proprietary elements would need to be disclosed to EPA, but would be withheld from the public if the person requesting protection for the confidential business information (CBI) demonstrates that the information is entitled to confidential treatment under 40 CFR part 2. Examples of proprietary components may include immunoassay reagents and antibodies and liquid phases in GC columns; e.g., DB-1®, SPB-octyl, Dexsil®, etc. A new or modified method submitted for EPA approval would need to include language stating that the proprietary reagent or instrument could be replaced by an equivalent. Changes made to the method after EPA approval would require the manufacturer to demonstrate, through supporting documentation, that the new proprietary equipment, substance, or reagent would produce results equal or superior to results produced with the material originally tested and on which the method approval is based. Additionally, EPA would not propose a method containing a proprietary reagent without accurate, specific instructions for handling the reagent and for safe disposal of each spent proprietary reagent and/or reaction product. When a material safety data sheet (MSDS) would need to accompany the proprietary material, the MSDS would be the appropriate vehicle to provide these instructions. Submission of a complete MSDS with a new method would satisfy EPA's need for instructions for safe handling and disposal of the reagent.

EPA recommends that developers of new methods that are proprietary consider Tier 1 validation because EPA cannot propose or promulgate (i.e., list in the CFR) new methods for nationwide use (i.e., Tier 2 or 3) in which all or a portion of the procedures used to determine the identity and concentration of the analyte(s) are considered confidential. EPA cannot approve these proprietary methods for nationwide use in compliance monitoring because if the entire method is CBI, it is unlikely that the public would have an adequate opportunity to comment on these procedures. Therefore, proprietary methods will not be approved through the rulemaking process whether they are Tier 1, 2, or 3 new methods, or Tier 2 or Tier 3 method modifications.